Hæmatologisk KFE
Aarhus Universitetshospital

Introduction letter

Clinical Research Unit,
Department of Haematology
Aarhus University Hospital

(hereafter called 'Site')

This Introduction letter details topics of interest to potential collaborators initiating contract negotiations. Further information can be obtained by contacting:

Preliminary Site Contact:

Senior Study Coordinator Tia Vetterli Sjøgren
Telephone: +45 3059 5320
E-mail: tiasjoeg@rm.dk

Contract Coordinator:

Manager Jens Kanstrup Kjær
Telephone: +45 4014 6452
E-mail: jenkja@rm.dk

The 'Introduction letter (version 3)' is approved **29-NOV-2017** by the Steering Committee and is referred to as 'local agreement' for all incoming sponsor initiated Clinical Trials.

Receipt date and name of recipient will be stored by site during the Clinical Trial

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Document History

Document version	Date of Approval	Summary of Change
3.1	01-OCT-2018	New contact information due to relocation
3.0	29-NOV-2017	General updates (page 3 - page 5) New pages (page 6 – page 8)
2.0	29-MAR-2017	General updates (page 3 - page 5) New pages (page 6 – page 8)
1.0 (original)	29-APR-2015	N.A.

The 'Introduction Letter' will be reviewed annually and a new version will be approved at least every two years. Appendix may be renewed more frequent according to local conditions.

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Introduction: Clinical Research Unit, Dept. of Haematology

The Site was formalized in 2002 and has expanded steadily with respect to both numbers of Clinical Trials as well as the size of staff.

As of **Nov-2017** the Site Staff includes 1 Senior Study Coordinator, 1 Manager, 7 Study Coordinators (SC), 1 Laboratory Coordinator. Currently, 75% of site personnel are self-financed.

The staff is continually updated in the latest developments in running clinical trials through formalized training including programs within ICH-GCP, IATA along with trial-specific and more commonly used EDC Systems (Electronic Data Capture). Needless to say, the personnel have a thorough and comprehensive knowledge and know-how within the quality assured health system of Aarhus University Hospital.

Clinical Trial experience includes:

- Commercial (Phase Ib – Phase IV) *Ongoing 10-20 enrolling trials*
- Non-Commercial (Phase Ib – Phase IV) *Ongoing 10-20 enrolling trials*

Besides the role as national coordinating site the office also accepts the role as a national core site.

Recent five-year Audit/Inspection activities include 3 Sponsor Audit (Sep-2014, Dec-14, Nov-16) and 1 DHMA/GCP Inspections (Dec-2014). Importantly, no major systematic errors have been detected.

The Site adheres to the principles of efficient and high-quality clinical trial management but has in addition to this developed and implemented several initiatives to improve local procedures, counting initiatives within these organisational areas:

- Strategically: 'Appoint and assign principles'. By specialising the Site Staff, each Clinical Trial is allocated to Study Coordinators based on their knowledge and experience within the actual field of haematological diseases and knowledge with the current investigational product.
- Tactical: Annual 'progress meetings' with collaborating departments ensure continuous exchange of new concepts, ideas and financial topics..
- Operational: 'Assisting tools' such as Standard Operating Procedures, flowcharts and guidelines support the daily Clinical Trial management. Off-Site, the 'Introduction Letter' and the budget assisting documents have proven helpful in facilitating the initial relations between Site and Sponsor/CRO.

The Department of Haematology has a long tradition of participation and leadership in a number of National, Nordic and International collaborative clinical trial study group, such as Nordic Lymphoma Group (NLG), Acute Leukaemia Group (ALG) and Nordic Myeloma Study Group (NMSG).

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Introduction: Preliminary activity and approval process

During Study Start-Up all initial contacts is through Senior Study Coordinator, Tia Vetterli Sjøgren, who ensures that collection and submission of preliminary documents, e.g. 'Feasibility' and 'Final Disclosure' and documents such as applicability/compliance assessment checklists or Source Data verification are completed in a timely fashion.

The Senior Study Coordinator is also responsible of coordinating meetings with the appointed PI at the Department for the collection of information requested by Sponsor. The initial meeting (Pre Study Visit, Pre Site-Selection Visit or similar) with Sponsor will also be planned through Senior Study Coordinator.

- Pre Study Visit (PSV) / Pre Site-Selection Visit (PSSV)

During the introductory meeting, the Clinical Research Unit will be represented with the appointed PI, Sub-Investigator (if appointed), Senior Study Coordinator, Contract Coordinator and a Study Coordinator with experience related to the Clinical Trial patient population or to the current investigational product. Here the Site will provide various certificates, specific documentation and guidelines during the meeting (CV, GCP, SOP, calibration and temperature documentation etc).

- Investigator Meetings

Site prioritises participation in Investigator Meetings highly. However, to accommodate local planning, we prefer a 12-week planning notice.

- Local Clinical Trial approval process

By 2016 new standards for implementation of Clinical Trials at Department of Haematology was initiated to uniform and expedite the start-up processes. Each process involved in approval of the Clinical Trial at Site is completed in a timely manner with respect to Sponsors timeframe. However, an estimated duration per procedure is not possible to state, as it rely on each Clinical Trial Agreement.

Table 1 show the order of the approval process including the representative(s) each process involves:

Approval process:	**Site representatives:**
Internal Review Board (IRB)[1,2]	Administrative heads and In-house sub-departments (Frequency: Q4W)
EC (if applicable)	Ethics Committee (Region Midtjylland)
DHMA (if applicable)	Danish Health and Medicines Authority
Budget	Contract Coordinator
Clinical Trial Agreement	Legal Advisors
Signature stage	Principal Investigator, Head of Department, Head of Research Unit, Head of Institute

TABLE 1: LOCAL CLINICAL TRIAL APPROVAL PROCESS

1: Before departmental approval the PI will complete a questionnaire intended for relevant in-house sub-departments. This serves to highlight the consequences of implementing the given protocol.

2: The subsequent approval of the protocol by the administrative heads of the department constitutes its final acceptance and acknowledges that contract and budget negotiation can be initiated.

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Clinical Trial Agreement: Site Procedures

The Clinical Trial Agreement (CTA) including budget drafts are to be forwarded to site contract coordinator, Manager Jens Kanstrup Kjær. Site has the following requests:

- The CTA is written and send in a Word format, track-changes enabled
- The budget will be provided in Excel format (preferably)
- The protocol and related documents and manuals are forwarded to Site to calculate the most accurate site budget.

Legal Wording

The Contract Coordinator at Site will forward the CTA to the Technology Transfer Office (TTO). TTO approval is mandatory and a TTO appointed legal advisor will contact the sponsor-assigned contact person with comments within 2-3 weeks.

All changes, both edited by site and sponsor, must be saved in track-changes versions. TTO will only be responsible for the approval of legal wording in the CTA, all financial concerns is to be approved by site contract coordinator.

Payment terms including payee information has to be completed before the CTA can be approved by Legal Advisor. Information will be completed by Contract Coordinator at Site.

Budget

The Contract Coordinator at Site will review the provided budget draft and make adjustments according to local mandatory regulations. To expedite negotiations with Sponsor, the Site budget drafts are accompanied by documentation sheet for financial transparency purposes.

Subcontracts

Collaboration with departments within Aarhus University Hospital as required by trial-specific assessments will be managed by sub-contracts from Site. Thus, the site budget will include both initial payments and standard item costs covering all trial-required expenses.

Frequent collaboration departments are Hospital Pharmacy, Department of Clinical Biochemistry, Department of Radiology, Department of Pathology and Department of Nuclear Medicine & PET-Centre.

If third party sub-contracts will be necessary, such agreements and payments will be held by Sponsor (e.g. Archiving of Study Material, Distribution of Pharmaceuticals)

Finalization and Site Initiation

The final approval from TTO will entail the signature phase to be initiated by Sponsor. Two (2) Wet-ink CTA originals are required by Site (Trial Master File & archival document for Aarhus University) in addition to Sponsor requirement. All originals will be forwarded to the Contract Coordinator at Site. The wet-ink version will be reviewed by Institute of Clinical Medicine to make sure the originals are identical with the approved document from TTO.

When CTA is fully signed and return to Sponsor the SIV can be completed. Before Site Initiation Visit, Sponsor/CRO makes sure that all study materials has been provided to Site (e.g. TMF, laboratory kits and other trial specific documents).

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Clinical Trial Agreement: Site requirements

During Site review of the Clinical Trial Agreement (CTA) standard logistical and financial topics will be discussed with Sponsor according to the following Site requirements:

- Reporting/Data Entry

Site will appoint one primary Study Coordinator (SC) and one assistant SC for each Clinical Trial. Only primary SC will perform data submission to relevant Case Report Forms (CRF). Due to daily workflow, the most efficient trial administration and reporting is managed by one SC only. In case Sponsor requires two 'primary' SC for Data entry and Query handling, the costs will be multiplied by two.

Data submission/entry for trial procedure will be entered into CRF within 7 business days after results have become available. In case of short-term illness or vacation by the staff, the data will be entered within 5 business days after the said sick leave. In case of long-term illness or long planned vacation (more than 3 weeks) the back-up will temporary perform data entry.

- The 'Contract Lifecycle'

The Clinical Trial Agreement is a long-term agreement. In case of new Sponsor initiatives or major protocol adjustments occur, Site will renegotiate relevant parts of the budget,

- Compensation/ Payment

Compensation due to participation in Clinical Trials primarily covers cost of local haematology examinations, time-consumption for all related study personnel and fixed expenses paid to collaborating departments. A list of most common costs is provided in appendix A: **'Clinical Trials – Compensation and Beneficiary Details'**.

- Access to Source Data

During Site Monitoring Visits (SMV), the Sponsor representative will access local data, however no access to Site Electronic Medical Record can be granted in accordance with regulations by the Region Midt judicial office. Please refer to appendix B: **'Electronic Data Capture'** for a general description.

- Calibration

For calibrations which are performed solely at the request of the Sponsor, and not being part of the recommended scheduled maintenance by service provider, Sponsor will reimburse Site for the actual cost for each calibration. A list of calibration procedures are provided in appendix C: **'Calibration procedures'**.

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Facility Details & Conditions: Frequently asked questions

GENERAL INFORMATION	
Address (research location):	Palle Juul-Jensens Boulevard 99, Entrance C, Level 1, C114. DK-8200 Aarhus N
Contact name(s):	Please refer to front page
Accreditation & Certificates:	DDKM (Danish Healthcare Quality Programme) GCP (Good Clinical Practice) *by individual training* IATA UN3373 & UN1845 (Dangerous Goods) *by individual training*
Curriculum Vitae:	Provided for Site delegates only. CV will only be signed when new CV information is applicable.
Facility Inspection possible?	Yes. During PSV/PSSV the Study Coordinator will be able to present local facilities. Notification preferably two days before the scheduled visit.

ADMINISTRATIVE PROCEDURES	
Protocol education:	1-2 initial education sessions with participation from all relevant medical staff, including physicians and nurses. Participation will be submitted to training log.
Patient screening:	Daily check by SC of all newly diagnosed and relapsed patients.
Clinical Trial Awareness:	The non-public electronic platform 'TrialFinder' will provide all necessary information from Clinical Trials.

STORAGE FACILITIES	
Freezer capacity:	-20 °C facility preferred. If site store samples more than 7 days, sponsor need a national approval for biobanking. -80 °C facility accessible, however limited storage capability only.
Non-freezer capacity:	5 °C (refrigerator, IMP); 18 °C (ambient, IMP); 25 °C (ambient, laboratory kits).
Other(s):	Centrifugation (refrigerated)
Quality Assurance:	24 hour temperature surveillance of storage facilities. Yearly calibration of both storage facilities and centrifuges.

MONITORING FACITIES	
Notification to Site:	4 weeks notices preferable.
Disposal resources:	Desk with internet access (WIFI)
IT accessibility:	Monitor must bring necessary IT equipment

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Facility Details & Conditions: Collaborating Departments

HOSPITAL PHARMACY*	
Address (main location):	Nørrebrogade 44, Building 17, DK-8000 Aarhus C
Contact name(s):	Will not be provided before Site Initiation Visit
Accreditation & Certificates:	DDKM (Danish Healthcare Quality Programme) DHMA (Danish Health and Medicines Authority)
Curriculum Vitae:	Will not be provided.
Facility Inspection possible?	Restricted access only. Before PSV/PSSV the Sponsor representative has to inform Senior Study Coordinator for facility inspection.
Summary of Product Characteristics (SPC):	If Sponsor chooses to supply a foreign registered drug and refers to the SPC and not to an Investigator Brochure it is Sponsor's responsibility to monitor upcoming SPC changes and to make sure that local Pharmacy always has valid SPC.
Receipt of Study drugs:	Verification of drug quality and release is mandatory when receiving trial specific drug products at either local Pharmacy or at a third party Company. No pharmaceuticals will be received at Site, unless it is approved for use in Denmark.
Removal of Study drugs:	Sponsor is responsible to alert local Pharmacy in case of recall of specific batches required by manufacturer. In case of recall of the foreign registered drug it is Sponsor's responsibility to make the recall known to the local Pharmacy immediately.

* Please refer to appendix D: '**Letter of Introduction**' for further information.

DEPARTMENT OF CLINICAL BIOCHEMISTRY	
Address (main location):	Palle Juul-Jensens Boulevard 99, Entr. C-2-C210, DK-8200 Aarhus N
Contact name(s):	Will not be provided. Contact through Study Coordinator only.
Accreditation & Certificates:	DDKM (Danish Healthcare Quality Programme) DANAK DEKS
Curriculum Vitae:	Will not be provided.
Facility Inspection possible?	Restricted access only. Before PSV/PSSV the Sponsor representative has to inform Senior Study Coordinator for facility inspection

DEPARTMENT OF RADIOLOGY	
Address (main location):	Palle Juul-Jensens Boulevard 99, Entr. C-5-C519, DK-8200 Aarhus N
Contact name(s):	Will not be provided. Contact through Study Coordinator only.
Accreditation & Certificates:	DDKM (Danish Healthcare Quality Programme)
Curriculum Vitae:	Will not be provided.
Facility Inspection possible?	No. Any facility topics will be forwarded by Study Coordinator.

DEPARTMENT OF PATHOLOGY	
Address (main location):	Palle Juul-Jensens Boulevard 99, Entr. F-1-C112, DK-8200 Aarhus N
Contact name(s):	Will not be provided. Contact through Study Coordinator only.
Accreditation & Certificates:	DDKM (Danish Healthcare Quality Programme)
Curriculum Vitae:	Will not be provided.
Facility Inspection possible?	No. Any facility topics will be forwarded by Study Coordinator.
Pathology Material:	No tissue block will be submitted to review, only slides
Pathology Report:	All reports will be available in Danish. Translation only accessible by translations-fee.

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